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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/784,589	02/23/2004	Lioudmila Tchistiakova	082181-36154	9597

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EXAMINER	
WANG, CHANG YU	
ART UNIT	**PAPER NUMBER**
1649	

DATE MAILED: 11/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/784,589	TCHISTIAKOVA ET AL.	
	Examiner	Art Unit	
	Chang-Yu Wang	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. Claims 1-7 are pending and under examination in this office action.

Information Disclosure Statement

2. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Specification

3. The specification is objected to because it contains sequences that need sequence identifiers on p 21, line 20, p. 73, line 27, p. 74, lines 3 and 11.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1 and 3-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a sequence comprising SEQ ID NO: 29 and some sequences listed in the table 14 binding to the VEGF receptor, does not reasonably provide enablement for variants and sequences comprising fragments with the sequence that represents the C-terminal thirteen amino acids of SEQ ID NO.7 to bind to VEGF receptor. In addition, while being enabling for the sequence of SEQ ID NO:29 and the sequences listed in the table 14 binding to VEGF receptor, does not reasonably provide enablement for inhibiting angiogenesis or vasculogenesis. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

6. "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is 'undue'. These factors include, but are not limited to:

(A) The breadth of the claims;

(B) The nature of the invention;

(C) The state of the prior art;

(D) The level of one of ordinary skill;

(E) The level of predictability in the art;

(F) The amount of direction provided by the inventor;

(G) The existence of working examples; and

(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)". See MPEP § 2164.01.

7. Claims 1 and 3-7 are drawn to a compound comprising an amino acid sequence that represents the C-terminal thirteen amino acids of SEQ ID NO:7, which encompass variants and sequences comprising fragments that could vary widely in structure and in function. Applicant has provided no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation. There is no guidance as to what could be changed and what could not be changed to preserve any common characteristics, for example, the positions that are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions to preserve particular activity. The specification fails to provide guidance of what elements are in common in the variants of the SEQ ID NO:7 that can bind to VEGF receptors. Furthermore, the specification has not disclosed this broad genus actually having the capability of blocking the interaction between VEGFs and VEGF receptors, and thus using as

pharmaceutical agents to inhibit angiogenesis or vasculogenesis. Although it has been shown that angiogenesis and vasculogenesis are commonly induced by VEGFs, there are some other molecules also capable of inducing angiogenesis and vasculogenesis, for example chemokines. CXCL8/IL8, one of the chemokines, is also a strong inducer of angiogenesis (see p. 485, the section of the chemokine system and angiogenesis. Roselilde et al.. APMIS. 2004. 112: 481-95). In addition, cyclooxygenase-2 and growth factors bFGF and TGF-β are also considered as angiogenic factors to induce angiogenesis (see p. 73 the first paragraph. Iniguez et al. Trends in Mol. Med. 2003. 9:73-78). Since the VEGFs are not the only factors being able to induce angiogenesis, blocking the interaction between VEGF and VEGF receptors does not necessarily inhibit angiogenesis. Because of the unpredictability of the invention and the lack of knowledge of function for each sequence, it would require undue experiments to use the invention commensurate in the scope with these claims.

8. Claims 1 and 3-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

9. To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or

chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this instant application, claims 1-7 are drawn to a genus, a composition comprising a sequence that represents the C terminal thirteen amino acid of ASn-X-X-Glu-Ile-Glu-X-X-X-Trp-X-X-X-X-X-Tyr (SEQ ID NO: 7), wherein X represents any amino acid. Applicant has not disclosed sufficient species for the broad genus of any peptides related to SEQ ID NO:7. While a generic sequence is provided, there is merely a set of common properties: there is no description of the conserved regions which are critical to the Flt-1 binding function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from other compounds are missing from the disclosure. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

10. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

The skilled artisan cannot envision the detailed chemical structure and function of the sequence that represents the C-terminal thirteen amino acids of SEQ ID NO:7, and

therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

11. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

12. Therefore, a compound comprising an amino acid sequence that represents the C-terminal thirteen amino acids of SEQ ID NO:7 and a compound comprising SEQ ID NO:29, have not met the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Obviousness-Type Non-Statutory Double Patenting

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA

1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. Claims 1-7 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 6733755 ('755) issued on May 11, 2004. Although the conflicting claims are not identical, they are not patentably distinct from each other because the sequence of the C-terminal thirteen amino acids of the SEQ ID NO:7 and the sequence of SEQ ID NO:29 in this instant case are encompassed in the sequences of the SEQ ID NOs:1-7 as stated in the claims as well as the specification of the '755. The compound comprising the peptides of SEQ ID NOs:1-7 in the '755 also includes the modified peptides of SEQ ID NOs:1-7 that remain VEGF receptor-binding function, which including the sequence of the C-terminal thirteen amino acids of the SEQ ID NO7 and the sequence of SEQ ID NO:29. Therefore, the claims 1-12 of the '755 meet the limitation of the instant claims. While not identical, the claims of the instant application and the '755 encompass the same scope of inventions. Thus the instant application are obvious over the claims 1-12 of the '755 which claim the same and non-distinct inventions of composition comprising the C-terminal thirteen amino acids of SEQ ID NO:7.

15. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

17. Claims 1 and 3-7 are rejected under 35 U.S.C. 102(b) as being anticipated by U. S. Patent No. 6,380,370 issued on April 30, 2002.

U. S. Patent No. 6,380,370 teaches the amino acids 77-89 of the SEQ ID NO:4025 meeting the limitation of the instant claim 1, which comprises an amino acid sequence that represents the C-terminal thirteen amino acids of SEQ ID NO:7. The sequence search results disclose as follows:

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US-09-134-001C-4025
; Sequence 4025, Application US/09134001C
; Patent No. 6380370
; GENERAL INFORMATION:
;  APPLICANT: Lynn Doucette-Stamm et al
;  TITLE OF INVENTION: NUCLEIC ACID AND AMINO ACID SEQUENCES
RELATING TO STAPHYLOCOCCUS
;  TITLE OF INVENTION:  EPIDERMIDIS FOR DIAGNOSTICS AND
THERAPEUTICS
;  FILE REFERENCE: GTC-007
;  CURRENT APPLICATION NUMBER: US/09/134,001C
;  CURRENT FILING DATE:  1998-08-13
;  PRIOR APPLICATION NUMBER: US 60/064,964
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;  PRIOR FILING DATE: 1997-11-08
;  PRIOR APPLICATION NUMBER: US 60/055,779
;  PRIOR FILING DATE: 1997-08-14
;  NUMBER OF SEQ ID NOS: 5674
; SEQ ID NO 4025
;   LENGTH: 106
;   TYPE: PRT
;   ORGANISM: Staphylococcus epidermidis
US-09-134-001C-4025

  Query Match             58.3%;  Score 28;  DB 3;  Length 106;
  Best Local Similarity   38.5%;  Pred. No. 19;
  Matches    5;  Conservative    0;  Mismatches    8;  Indels
0;  Gaps    0;

Qy          4 EIEXXXWXXXXXY 16
              |||   |     |
Db         77 EIENSKWASVTFY 89
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18. Therefore, Claims 1 and 3-7 are anticipated by U. S. Patent No. 6380370.

Conclusion

NO CLAIM IS ALLOWED.

19. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

20. Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with

the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang, Ph.D. whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, Ph.D., can be reached at (571) 272-0867.

22. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CYW
November 8, 2005

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER